

DOCKET NO.: CEPH-0939
wherein:

PATENT

TECH CENTER 1600/2900

SEP 25 2002

RECEIVED



ring B and ring F, independently, and each together with the carbon atoms to which they are attached, are selected from the group consisting of:

- a) an unsaturated 6-membered carbocyclic aromatic ring in which from 1 to 3 carbon atoms may be replaced by nitrogen atoms;
- b) an unsaturated 5-membered carbocyclic aromatic ring; in which, optionally, either
 - 1) one carbon atom is replaced with an oxygen, nitrogen, or sulfur atom;
 - 2) two carbon atoms are replaced with a sulfur and a nitrogen atom, an oxygen and a nitrogen atom, or two nitrogen atoms; or
 - 3) three carbon atoms are replaced with three nitrogen atoms;

R¹ is selected from the group consisting of:

- a) H, substituted or unsubstituted alkyl having from 1 to 4 carbons, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, or substituted or unsubstituted heteroarylalkyl;



DOCKET NO.: CEPI-0939

PATENT

TECH CENTER 1600/2900

SEP 25 2002

RECEIVED

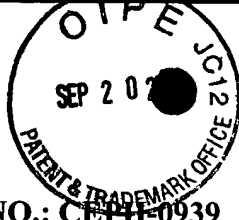
- b) $-C(=O)R^9$, where R^9 is selected from the group consisting of alkyl, aryl and heteroaryl;
- c) $-OR^{10}$, where R^{10} is selected from the group consisting of H and alkyl having from 1 to 4 carbons;
- d) $-C(=O)NH_2$, $-NR^{11}R^{12}$, $-(CH_2)_pNR^{11}R^{12}$, $-(CH_2)_pOR^{10}$, $-O(CH_2)_pOR^{10}$ and $-O(CH_2)_pNR^{11}R^{12}$, wherein p is from 1 to 4; and wherein either
- 1) R^{11} and R^{12} are each independently selected from the group consisting of H and alkyl having from 1 to 4 carbons; or
 - 2) R^{11} and R^{12} together form a linking group of the formula $-(CH_2)_2-X^1-(CH_2)_2-$, wherein X^1 is selected from the group consisting of $-O-$, $-S-$, and $-CH_2-$;

R^2 is selected from the group consisting of H, alkyl having from 1 to 4 carbons, $-OH$, alkoxy having from 1 to 4 carbons, $-OC(=O)R^9$, $-OC(=O)NR^{11}R^{12}$, $-O(CH_2)_pNR^{11}R^{12}$, $-O(CH_2)_pOR^{10}$, substituted or unsubstituted arylalkyl having from 6 to 10 carbons, and substituted or unsubstituted heteroarylalkyl;

R^3 , R^4 , R^5 and R^6 are each independently selected from the group consisting of:

- a) H, aryl, heteroaryl, F, Cl, Br, I, $-CN$, CF_3 , $-NO_2$, $-OH$, $-OR^9$, $-O(CH_2)_pNR^{11}R^{12}$, $-OC(=O)R^9$, $-OC(=O)NR^{11}R^{12}$, $-O(CH_2)_pOR^{10}$, $-CH_2OR^{10}$, $-NR^{11}R^{12}$, $-NR^{10}S(=O)R^9$, $-NR^{10}C(=O)R^9$,
- b) $-CH_2OR^{14}$, wherein R^{14} is the residue of an amino acid after the hydroxyl group of the carboxyl group is removed;
- c) $-NR^{10}C(=O)NR^{11}R^{12}$, $-CO_2R^2$, $-C(=O)R^2$, $-C(=O)NR^{11}R^{12}$, $-CH=NOR^2$, $-CH=NR^9$, $-(CH_2)_pNR^{11}R^{12}$, $-(CH_2)_pNHR^{14}$, or $-CH=NNR^{2A}R^{2A}$ wherein R^{2A} is the same as R^2 ;
- d) $-S(O)_yR^2$, $-(CH_2)_pS(O)_yR^9$, $-CH_2S(O)_yR^{14}$ wherein y is 0, 1 or 2;
- e) alkyl having from 1 to 8 carbons, alkenyl having from 2 to 8 carbons, and alkynyl having 2 to 8 carbons, wherein

- 1) each alkyl, alkenyl, or alkynyl group is unsubstituted; or



RECEIVED

SEP 25 2002

DOCKET NO.: CEFH-0939

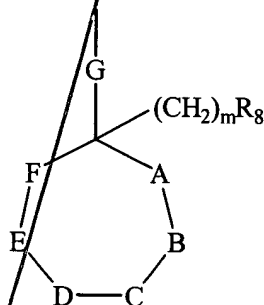
TECH CENTER 1600/2800

PATENT

2) each alkyl, alkenyl or alkynyl group is substituted with 1 to 3 groups selected from the group consisting of aryl having from 6 to 10 carbons, heteroaryl, arylalkoxy, heterocycloalkoxy, hydroxylalkoxy, alkoxyalkoxy, hydroxyalkylthio, alkoxy-alkylthio, F, Cl, Br, I, -CN, -NO₂, -OH, -OR⁹, -X²(CH₂)_pNR¹¹R¹², -X²(CH₂)_pC(=O)NR¹¹R¹², -X²(CH₂)_pOC(=O)NR¹¹R¹², -X²(CH₂)_pCO₂R⁹, X²(CH₂)_pS(O)_yR⁹, -X²(CH₂)_pNR¹⁰C(=O)NR¹¹R¹², -OC(=O)R⁹, -OCONHR², -O-tetrahydropyranyl, -NR¹¹R¹², -NR¹⁰CO₂R⁹, -NR¹⁰C(=O)NR¹¹R¹², -NHC(=NH)NH₂, NR¹⁰C(=O)R⁹, -NR¹⁰S(O)₂R⁹, -S(O)_yR⁹, -CO₂R², -C(=O)NR¹¹R¹², -C(=O)R², -CH₂OR¹⁰, -CH=NNR²R^{2A}, -CH=NOR², -CH=NR⁹, -CH=NNHCH(N=NH)NH₂, -S(=O)₂NR²R^{2A}, -P(=O)(OR¹⁰)₂, -OR¹⁴, and a monosaccharide having from 5 to 7 carbons wherein each hydroxyl group of the monosaccharide is independently either unsubstituted or is replaced by H, alkyl having from 1 to 4 carbons, alkylcarbonyloxy having from 2 to 5 carbons, or alkoxy having from 1 to 4 carbons;

X² is O, S, or NR¹⁰;

R⁷ is



wherein:

m is 0-4;

G is a bond; or alkylene having 1 to 4 carbons, wherein the alkylene group is unsubstituted, or substituted with NR^{11A}R^{12A} or OR¹⁹;



DOCKET NO.: CEPH-0939

PATENT

TECH CENTER 1600/2900

SEP 25 2002

RECEIVED

R^{11A} and R^{12A} are the same as R^{11} and R^{12} ;

R^{19} is selected from the group consisting of H, alkyl, acyl, and $C(=O)NR^{11A}R^{12A}$;

R^8 is selected from the group consisting of $O(C=O)NR^{11}R^{12}$, -CN, acyloxy, alkenyl, $-O-CH_2-O-(CH_2)_2-O-CH_3$, halogen and R^{1A} wherein R^{1A} is the same as R^1 ;

A and B are independently selected from the group consisting of O, N, S, CHR^{17} , $C(OH)R^{17}$, $C(=O)$, and $CH_2=C$; or A and B together can form $-CH=CH-$;

C and D are independently selected from the group consisting of a bond, O, N, S, CHR^{17} , $C(OH)R^{17}$, $C(=O)$ and $CH_2=C$;

E and F are independently selected from the group consisting of a bond, O, N, S, $C(=O)$, and $CH(R^{17})$;

R^{17} is selected from the group consisting of H, substituted or unsubstituted alkyl, alkoxy carbonyl, and substituted or unsubstituted alkoxy;

wherein:

- 1) ring J contains 0 to 3 ring heteroatoms;
- 2) any two adjacent hydroxyl groups of ring J can be joined in a dioxolane ring;
- 3) any two adjacent ring carbon atoms of ring J can be joined to form a fused aryl or heteroaryl ring;
- 4) any two adjacent ring nitrogen atoms of ring J can be joined to form a fused heterocyclic ring which can be substituted with 1 to 3 alkyl or aryl groups;

provided that:

- 1) ring J contain at least one carbon atom that is saturated;
- 2) ring J not contain two adjacent ring O atoms;
- 3) ring J contains a maximum of two ring $C(=O)$ groups;
- 4) when G is a bond, ring J can be heteroaryl;

Q is selected from the group consisting of O, S, NR^{13} , NR^{7A} wherein R^{7A} is the same as R^7 , CHR^{15} , $\text{X}^3\text{CH}(\text{R}^{15})$, and $\text{CH}(\text{R}^{15})\text{X}^3$, wherein X^3 is selected from the group consisting of BO- , -S- , $\text{-CH}_2\text{-}$, NR^{7A} , and NR^{13} ;

W is selected from the group consisting of CR^{18}R^7 and CHR^{50} where R^{50} is alkyl having from 1 to 4 carbons, -OH , alkoxy having from 1 to 4 carbons, -OC(=O)R^9 , $\text{-OC(=O)NR}^{11}\text{R}^{12}$, $\text{-O(CH}_2)_p\text{NR}^{11}\text{R}^{12}$, $\text{-O(CH}_2)_p\text{OR}^{10}$, substituted or unsubstituted arylalkyl having from 6 to 10 carbons, and substituted or unsubstituted heteroarylalkyl;

R^{13} is selected from the group consisting of H , $\text{-SO}_2\text{R}^9$, $\text{-CO}_2\text{R}^9$, -C(=O)R^9 , $\text{-C(=O)NR}^{11}\text{R}^{12}$, alkyl of 1-8 carbons, alkenyl having 2-8 carbons, and alkynyl having 2-8 carbons; and either

1) the alkyl, alkenyl, or alkynyl group is unsubstituted; or

2) the alkyl, alkenyl, or alkynyl group independently is substituted

with 1 to 3 groups selected from the group consisting of aryl having from 6 to 10 carbons, heteroaryl, arylalkoxy, heterocycloalkoxy, hydroxylalkoxy, alkyloxy-alkoxy, hydroxyalkylthio, alkoxy-alkylthio, F, Cl, Br, I, -CN , -NO_2 , -OH , -OR^9 , $\text{-X}^2(\text{CH}_2)_p\text{NR}^{11}\text{R}^{12}$, $\text{-X}^2(\text{CH}_2)_p\text{C(=O)NR}^{11}\text{R}^{12}$, $\text{-X}^2(\text{CH}_2)_p\text{OC(=O)NR}^{11}\text{R}^{12}$, $\text{-X}^2(\text{CH}_2)_p\text{CO}_2\text{R}^9$, $\text{-X}^2(\text{CH}_2)_p\text{S(O)}_y\text{R}^9$, $\text{-X}^2(\text{CH}_2)_p\text{NR}^{10}\text{C(=O)NR}^{11}\text{R}^{12}$, -OC(=O)R^9 , -OCONHR^2 , $\text{-O-tetrahydropyranyl}$, $\text{-NR}^{11}\text{R}^{12}$, $\text{-NR}^{10}\text{CO}_2\text{R}^9$, $\text{-NR}^{10}\text{C(=O)NR}^{11}\text{R}^{12}$, -NHC(=NH)NH_2 , $\text{NR}^{10}\text{C(=O)R}^9$, $\text{-NR}^{10}\text{S(O)}_2\text{R}^9$, $\text{-S(O)}_y\text{R}^9$, $\text{-CO}_2\text{R}^2$, $\text{-C(=O)NR}^{11}\text{R}^{12}$, -C(=O)R^2 , $\text{-CH}_2\text{OR}^{10}$, $\text{-CH=NNR}^2\text{R}^{2A}$, -CH=NOR^2 , -CH=NR^9 , $\text{-CH=NNHCH(N=NH)NH}_2$, $\text{-S(=O)}_2\text{NR}^2\text{R}^{2A}$, $\text{-P(=O)(OR}^{10})_2$, -OR^{14} , and a monosaccharide having from 5 to 7 carbons wherein each hydroxyl group of the monosaccharide is independently either unsubstituted or is replaced by H, alkyl having from 1 to 4 carbons, alkylcarbonyloxy having from 2 to 5 carbons, or alkoxy having from 1 to 4 carbons;

R^{15} is selected from the group consisting of H, OR^{10} , SR^{10} , R^{7A} , and R^{16} ;

R^{16} is selected from the group consisting of alkyl of 1 to 4 carbons; phenyl; naphthyl;

arylalkyl having 7 to 15 carbons, $-\text{SO}_2\text{R}^9$, $-\text{CO}_2\text{R}^9$, $-\text{C}(=\text{O})\text{R}^9$, alkyl having 1-8 carbons; alkenyl having 2 to 8 carbons, and alkynyl having 2 to 8 carbons, wherein

1) each alkyl, alkenyl, or alkynyl group is unsubstituted; or

2) each alkyl, alkenyl, or alkynyl group is substituted with 1 to 3

groups selected from the group consisting of aryl having from 6 to 10 carbons, heteroaryl, arylalkoxy, heterocycloalkoxy, hydroxylalkoxy, alkoxy-alkoxy, hydroxyalkylthio, alkoxy-alkylthio, F, Cl, Br, I, -CN, -NO₂, -OH, -OR⁹, -X²(CH₂)_pNR¹¹R¹², -X²(CH₂)_pC(=O)NR¹¹R¹², -X²(CH₂)_pOC(=O)NR¹¹R¹², -X²(CH₂)_pCO₂R⁹, X²(CH₂)_pS(O)_yR⁹, -X²(CH₂)_pNR¹⁰C(=O)NR¹¹R¹², -OC(=O)R⁹, -OCONHR², -O-tetrahydropyranyl, -NR¹¹R¹², -NR¹⁰CO₂R⁹, -NR¹⁰C(=O)NR¹¹R¹², -NHC(=NH)NH₂, NR¹⁰C(=O)R⁹, -NR¹⁰S(O)₂R⁹, -S(O)_yR⁹, -CO₂R², -C(=O)NR¹¹R¹², -C(=O)R², -CH₂OR¹⁰, -CH=NNR²R^{2A}, -CH=NOR², -CH=NR⁹, -CH=NNHCH(N=NH)NH₂, -S(=O)₂NR²R^{2A}, -P(=O)(OR¹⁰)₂, -OR¹⁴, and a monosaccharide having from 5 to 7 carbons wherein each hydroxyl group of the monosaccharide is independently either unsubstituted or is replaced by H, alkyl having from 1 to 4 carbons, alkylcarbonyloxy having from 2 to 5 carbons, or alkoxy having from 1 to 4 carbons;

R¹⁸ is selected from the group consisting of R², thioalkyl of 1-4 carbons, and halogen;

A¹ and A² are selected from the group consisting of H, H; H, OR²; H, -SR²; H, -N(R²)₂; and a group wherein A¹ and A² together form a moiety selected from the group consisting of =O, =S, and =NR²;

B¹ and B² are selected from the group consisting of H, H; H, -OR²; H, -SR²; H, -N(R²)₂; and a group wherein B¹ and B² together form a moiety selected from the group consisting of =O, =S, and =NR²; with the proviso that at least one of the pairs A¹ and A², or B¹ and B², form =O;

with the proviso that when Q is NH or NR^{7A}, and in any R⁷ or R^{7A} group m is 0 and G is a bond, R⁸ is H, and R⁷ or R^{7A} contains one ring hetero oxygen atom at position A in a 5- or



DOCKET NO. 64641-0939

PATENT

A1
cont

6-membered ring, then B cannot be CHR^{17} where R^{17} is substituted or unsubstituted alkyl; and

with the further proviso that the compound of Formula I contains one R^7 or R^{7A} group or both an R^7 and R^{7A} group.

TECH CENTER 1600/2900

SEP 25 2002

RECEIVED

41. (Amended) The compound of claim 37 wherein the constituent variables of the compounds of Formula II are selected in accordance with the following table:

A2

A1A2	B1B2	R3	A	B	C	D	E	F
H2	O	H	O	CH2	bond	bond	bond	bond
H2	O	H	O	CH2	bond	bond	bond	bond
H2	O	H	O	CH2	bond	bond	bond	bond
H2	O	H	C(OH)	CH2	CH2	bond	bond	bond
H2	O	3-Br	O	CH2	bond	bond	bond	bond
H2	O	3-CH2OCH2-CH3	O	CH2	bond	bond	bond	bond
H2	O	3-CH2OCH2-CH2OCH3	O	CH2	bond	bond	bond	bond
H2	O	H	O	CH2	CH2	CH2	CH2	bond
H2	O	H	CH2	O	CH2	CH2	CH2	bond

A3

64. (Amended) A pharmaceutical composition for treating prostate disorders comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

A4

73. (Amended) A method for treating prostate disorders which comprises administering to a host in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1.

Please add new claim 95:

A5

--95. (New) The compound of claim 21 wherein R^1 , R^3 , R^4 and R^6 are each H; A_1, A_2 is H, H; B_1, B_2 is =O; Q is NH; R^5 is H or alkoxy; W is CR^{18}R^7 where R^{18} is H; G is a bond; m is 1; R^8 is OH or $-\text{C}(=\text{O})\text{R}^9$ where R^9 is alkyl; A is O; B, C and D are each CHR^{17} where R^{17} is H; and E and F are each a bond.--